CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
2-BROMO-4-HYDROXY-ACETOPHENONE

Chemical Code # 969, Tolerance # 51573
SB 950 # 540
Original date: October 10, 2002

I. DATA GAP STATUS

Chronic toxicity, rat:	Data Gap, no study on file.
Combined, rat:	Data Gap, no study on file.
Chronic toxicity, rat:	Data Gap, no study on file.
Chronic toxicity, dog:	Data Gap, no study on file.
Oncogenicity, rat:	Data Gap, no study on file.
Oncogenicity, mouse:	Data gap, no study on file
Reproduction, rat:	Data gap, no study on file.
Teratology, rat:	Data Gap, inadequate study, no adverse effect indicated.
Teratology, rabbit:	Data Gap, no study on file.
Gene mutation:	No data gap, no adverse effect
Chromosome effects:	No data gap, no adverse effect
DNA damage:	Data gap, inadequate study, no adverse effect indicated.
Neurotoxicity:	Not required at this time.

Toxicology one-liners are attached.

All record numbers through 132360 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.

File name: T021010
Original: J. Kishiyama and Gee, October 10, 2002

BHAP is a non-food use antimicrobial. The US EPA issued a “Reregistration Eligibility Decision (RED)” in February of 1995.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

CHRONIC TOXICITY, RAT

No study on file.

Subchronic:

51573 - 006 132360 Tompkins, E. C. "A 90-Day Oral Toxicity Study of BHAP in Rats with Four Week Recovery Period." **(** WIL Research Laboratories, Inc.,WIL-94050, June 30, 1994.) BHAP, purity 31.9%, batch 2365, was administered via gavage at doses of 0 (corn oil), 6, 30, or 60 mg/kg/day (not adjusted for purity) to 10 Crl:CD®BR rats/sex/group with ten additional control and high dose animals/sex for a 4-week recovery period. BHAP at the high dose of 60 mg/kg resulted in mortality and, therefore, the dose was lowered to 45 mg/kg/day at week seven. Suppurative inflammation of the trachea in some mid and high dose males and females was considered partially responsible for the high mortality. Clinical signs of gasping, labored breathing and, especially, rales were observed in the mid and high dose groups. Other clinical signs included decreased defecation, salivation, and nasal discharge. Body weight and food consumption for high dose males were lower although females were comparable to controls. Testes weights were decreased for mid and high dose males at week 13 but not for the high dose recovery group at week 17. With a limited number of survivors at week 17 for the high dose, the symptomatic effects on the trachea were no longer found. There were no treatment-related effects on hematology, clinical chemistry, urinalysis or ophthalmology. NOEL = 6 mg/kg/day (clinical signs). UNACCEPTABLE, upgradeable (clarification of the test article content and whether it was technical grade). (Kishiyama and Gee, 10/9/02).

CHRONIC TOXICITY, DOG

No study on file.

ONCOGENICITY, RAT

No study on file.

ONCOGENICITY, MOUSE

No study on file.

REPRODUCTION, RAT

No study on file.

TERATOLOGY, RAT

51573 - 003 114096 Rodwell, D. E. "A Teratology Study in Rats with BHAP." (WIL Research Laboratories, Inc., Project No.: WIL-94018, March 27, 1987.) BHAP (purity 31.9%, batch 1785) was administered via gavage at doses of 0 (corn oil/1% Tween® 80), 10, 30, or 100 mg/kg/day to 25 bred Sprague-Dawley COBS® CD® rats/group during gestation days 6 through 15. Statistically significantly reduced food consumption was recorded for high-dose group days 12 through 20 and for the mid-dose group, days 12 - 16 (19 g/animal/day versus 22 for controls) Some high dose animals exhibited respiratory rales both pre-dose and post-dose and a few had yellow and/or clear material around the mouth. Maternal NOEL = 30 mg/kg (clinical signs, lower food consumption) There was no evidence of developmental toxicity. Developmental NOEL = 100 mg/kg. UNACCEPTABLE. Upgradeable (rationale for dose selection with range-finding study (WIL-94017), justification for the test article at approximately 30%). (Kishiyama and Gee, 10/9/02)

TERATOLOGY, RABBIT

No study on file.

GENE MUTATION

51573 - 001 064023 Sernau, R. C., Study Director. "CHO/HGPRT Forward Mutation Assay: BHAP: Final Report." (Hazleton Biotechnologies Corp., HBC Project No: 197-185, October 8, 1985.) BHAP, purity assumed 100%, specific gravity = 1.25, was evaluated for potential mutagenicity at concentrations of 0, 0.5, 1.0, 2.5 , 5.0, and 7.5 : g/ml without activation and at 0, 2.5, 5.0, 7.5, 10 and 25 : g/ml in the presence of metabolic activation (source not stated). There were duplicate cultures in the single trial. Exposure time to Chinese hamster ovary cells was for 5 hours, followed by an eight-day expression period before plating for 6-thioguanine resistance (5 plates per initial culture). BHAP exposure did not increase mutation frequency compared with negative controls. Positive controls were functional. UNACCEPTABLE, not upgradeable (single trial). Also, the test article was not defined, other than as a black liquid. (Kishiyama and Gee, 9/24/02).

** 51573 - 001 064026 Cavagnaro, J., Study Director. "Mutagenicity Evaluation of BHAP Lot # GLB62985 in the Ames Salmonella/Microsome Plate Assay." (Hazleton Biotechnologies Corp., HB Project No.: 20988, December 1985.) BHAP was evaluated for potential mutagenicity at concentrations of 0 (DMSO), 0.12, 0.37, 1.1, 3.3, and 10 : g/plate with and without rat liver metabolic activation using *Salmonella* strains TA98, TA100, TA1535, TA1537 and TA1538. There were triplicate plates per concentration with a single trial. Test article exposure time was forty-eight hours. BHAP treatment with and without S9 Mix did not increase the number of revertants relative to the solvent control. Positive controls were functional. ACCEPTABLE. (Kishiyama and Gee, 10/8/02).

CHROMOSOME EFFECTS

** 51573 - 001 064025 Ivett, J. L., Study Director. "Clastogenic Evaluation of BHAP Lot No. GLB62985 in the *In Vivo* Mouse Micronucleus Assay." (Hazleton Biotechnologies Corp., HB Project No: 20996, February 1986.) BHAP, purity assumed 100% (density = 1.30 g/ml), was evaluated for the potential to induce micronuclei in bone marrow polychromatic erythrocytes in ICR strain mice, 5/sex/group, with a single (IP) injection at doses of 0 (corn oil), 70, 233 or 700 mg/kg. Animals were sacrificed at 24, 48 or 72 hours after treatment. BHAP treatment under study conditions did not significantly increase micronuclei in bone marrow erythrocytes. ACCEPTABLE. (Kishiyama and Gee, 10/7/02)

DNA DAMAGE

51573 - 001 064024 Sernau, R. C., Study Director. "Unscheduled DNA Synthesis Rat Hepatocyte Assay with BHAP." (Hazleton Biotechnologies Corp., HBC Project No: 197-186, December 5, 1985.) BHAP, purity assumed 100%, lot GLB62985, was evaluated for induction of unscheduled DNA synthesis in male rat liver hepatocytes at concentrations of 0 (DMSO)0.1, 0.25, 0.5, 1, and 2 : g/ml in duplicate cultures by autoradiography. Test article exposure time was "overnight" (actual time was not specified). BHAP treatment did not significantly increase nuclear grain counts. UNACCEPTABLE. Upgradeble (no individual data including cytoplasmic

counts, nuclear counts and actual exposure time). (Kishiyama and Gee, 10/7/02).

NEUROTOXICITY

Not required at this time.

OTHERS:

STUDY NOT ON FILE: “21-Day dermal toxicity study in rabbits with BHAP.” (Adam, G., WIL Research Laboratories, Project WIL-94021, 1987). This study should be submitted for review. (Gee, 10/10/02).